



California State Board of Pharmacy

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STATE AND CONSUMER SERVICES AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GRAY DAVIS, GOVERNOR

May 25, 2004

TO: ALL INTERESTED PARTIES

RE: PROPOSED ADDITION OF TITLE 16, SECTION 1751 ET SEQ., STERILE COMPOUNDING

In response to comments received from the Office of Administrative Law and the Building Standards Commission, the board is proposing to amend text of the proposed regulation regarding sterile injectable compounding standards. Changes to the final text of the regulation that was disapproved by the Office of Administrative Law are indicated in the accompanying text with ***bold italics*** denoting additions and double ~~strikeout~~ denoting deletions. These modifications are needed to eliminate the inclusion of building standards which cannot be adopted by the board.

The board will vote on these changes at its July 21-22, 2004 meeting.

The board is required to make available the proposed language for at least 15 days. Written comments regarding the latest proposed amendments must be sent to the board postmarked no later than June 11, 2004.

Written comments should be sent to the board at:

Board of Pharmacy
Attn: Paul Riches
400 R Street, Suite 4070
Sacramento, CA 95814

Comments may also be emailed to Paul_Riches@dca.ca.gov, or faxed to (916) 327-6308. Comments received by email or fax must contain the name and address of the commenter.

Attachment

Board of Pharmacy
Proposed Revisions to Title 16 CCR 1751 et seq.
May 25, 2004

*- Revisions noted with additions in ***bold italics*** and deletions noted in ~~double-strikeout~~

Article 7. Sterile Injectable Compounding

Amend Section 1751. Sterile Injectable Compounding Area. ~~for Parenteral Solutions.~~

(a) ~~The pharmacy shall have a designated area for the preparation of sterile injectable products for dispensing which shall meet the following standards:~~

~~(a) (1) Clean Room and Work Station Requirements, shall be in accordance with Section 490A.3.1 2-714(g)(1) of Title 24, Part 2, Chapter 4A of the California Code of Regulations Administrative Code.~~

~~(b) (2) Walls, ceilings and floors shall have cleanable, nonporous surfaces and be constructed be in accordance with Section 490A.3 2-714(g)(2) of Title 24, Part 2, Chapter 4A of the California Code of Regulations Administrative Code.~~

~~(c) (3) Be ventilated in a manner in accordance with Section 505.12 4-1105(d) of Title 24, Part 4, Chapter 5 of the California Code of Regulations Administrative Code.~~

~~(d) (4) Be certified annually by a qualified technician who is familiar with the methods and procedures for certifying laminar air flow hoods and clean room requirements, in accordance with standards adopted by the Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, United States General Services Administration, as amended May 30, 1976 (available from the U.S. General Services Administration, Specifications Activity, Printed Materials Supply Division, Building 197, Naval Weapons Plant, Washington, D.C. 20407). Certification records must be retained for at least 3 years.~~

~~(e) (5) The pharmacy shall be arranged in accordance with Section 490A.3 2-714(g)(3) of Title 24, Part 2, Chapter 4A of the California Code of Regulations Administrative Code. Items related to the compounding of sterile injectable products parenteral solutions within the compounding area may not be stored in corrugated cardboard boxes and shall be stored in such a way as to maintain the integrity of an aseptic environment.~~

~~(f) (6) A sink with hot and cold running water shall be included in accordance in Section 490A.3.4 2-714(g)(4) of Title 24, Part 2, Chapter 4A of the California Code of Regulations Administrative Code.~~

~~(g) (7) There shall be a refrigerator and/or freezer of sufficient capacity to meet the storage requirements for all material requiring refrigeration.~~

NOTE:

Authority cited: Section 4005, Business and Professions Code.

Reference: Section 4005, Business and Professions Code; and Section 18944(a), Health and Safety Code.

Add Section 1751.01 Facility and Equipment Standards for Sterile Injectable Compounding from Non-Sterile Ingredients.

~~(a) On and after January 1, 2005 this subdivision shall apply to any pharmacy compounding sterile injectable products from one or more non-sterile ingredients. The aseptic processing of such products shall occur in one of the following environments:~~

- ~~(1) A class 100 laminar airflow hood within a class 10,000 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas.~~
~~(2) A class 100 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas.~~
~~(3) A barrier isolator that provides a class 100 environment for compounding.~~
~~(b)~~ No sterile injectable product shall be prepared if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures for the safe compounding of sterile injectable drug products.
~~(e)~~ ~~(b)~~ During the preparation of sterile injectable products, access to the designated area or cleanroom must be limited to those individuals who are properly attired.
~~(d)~~ ~~(c)~~ All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected.
~~(e)~~ ~~(d)~~ Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools, must be disinfected weekly and after any unanticipated event that could increase the risk of contamination.

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code; and Section 18944(a), Health and Safety Code.

Add Section 1751.02. Policies and Procedures.

- (a) Written policies and procedures associated with the pharmacy's preparation and dispensing of sterile injectable products shall include, but not be limited to:
- (1) Compounding, filling, and labeling of sterile injectable compounds.
 - (2) Labeling of the sterile injectable product based on the intended route of administration and recommended rate of administration.
 - (3) Equipment and supplies.
 - (4) Training of staff in the preparation of sterile injectable products.
 - (5) Procedures for handling cytotoxic agents.
 - (6) Quality assurance program.
 - (7) Record keeping requirements.
- (b) The ingredients and the compounding process for each preparation must be determined in writing before compounding begins and must be reviewed by a pharmacist.
- (c) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following:
- (1) All written policies and procedures shall be immediately available to all personnel involved in these activities and board inspectors.
 - (2) All personnel involved must read the policies and procedures before compounding sterile injectable products, and any additions, revisions, and deletions to the written policies and procedures must be communicated to all personnel involved in sterile compounding.
 - (3) Policies and procedures must address at least the following:
 - (A) Competency evaluation.
 - (B) Storage and handling of products and supplies.
 - (C) Storage and delivery of final products.
 - (D) Process validation.

- (E) Personnel access and movement of materials into and near the controlled area.
- (F) Use and maintenance of environmental control devices used to create the critical area for manipulation of sterile products (e.g., laminar-airflow workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator workstations).
- (G) Regular cleaning schedule for the controlled area and any equipment in the controlled area and the alternation of disinfectants. Pharmacies subject to an institutional infection control policy may follow that policy as it relates to cleaning schedules and the alternation of disinfectants in lieu of complying with this subdivision.
- (H) Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area.
- (I) For sterile batch compounding, written policies and procedures must be established for the use of master formulas and work sheets and for appropriate documentation.
- (J) Sterilization.
- (K) End-product evaluation and testing.

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.2. Labeling Requirements.

In addition to existing labeling requirements, a pharmacy which compounds sterile parenteral injectable products shall include the following information on the labels for those products:

- a. Telephone number of the pharmacy, except for sterile injectable products dispensed for inpatients of a hospital pharmacy.
- b. Name and concentrations of ~~all~~ ingredients contained in the sterile injectable parenteral product ~~including primary solution.~~
- c. Instructions for storage and handling.
- d. All cytotoxic agents shall bear a special label which states “Chemotherapy-Dispose of Properly.”

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.3. Recordkeeping Requirements.

~~Pharmacies which both compound parenteral solutions and dispense those solutions shall have on the premises or readily accessible a patient record for each patient being treated with parenteral therapy. In addition to existing recordkeeping requirements, the following records shall be maintained:~~

- ~~(a) Records of furnishing of all prescriptions and medical supplies;~~
- ~~(b) Information relevant to the patient's parenteral therapy shall include but not be limited to:~~
 - ~~(1) Patient's name, age, sex, address, and body weight.~~

- ~~(2) Primary diagnosis related to need for prescribed therapy; secondary diagnosis if available.~~
- ~~(3) Summary of most recent hospitalization and/or previous history.~~
- ~~(4) Medication history, including current diet/medication regimen and drug/food allergies.~~
- ~~(c) Progress notes documenting contact with the patient or physician relative to parenteral therapy.~~
- ~~(d) Laboratory data relevant to parenteral therapy.~~
- (a) Pharmacies compounding sterile injectable products for future use pursuant to section 1716.1 shall, in addition to those records required by section 1716.2, have records indicating the name, lot number, amount, and date on which the products were provided to a prescriber.
- (b) In addition to the records required by subdivisions (a), for sterile products compounded from one or more non-sterile ingredients the following records must be maintained for at least three years:
 - (1) The training and competency evaluation of employees in sterile product procedures.
 - (2) Refrigerator and freezer temperatures.
 - (3) Certification of the sterile compounding environment.
 - (4) Other facility quality control logs specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment).
 - (5) Inspection for expired or recalled pharmaceutical products or raw ingredients.
 - (6) Preparation records including the master work sheet, the preparation work sheet, and records of end-product evaluation results.
- (c) Pharmacies shall maintain records of validation processes as required by Section 1751.7 (b) for three years.

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.4. ~~Protective Clothing~~ Attire.

- (a) When preparing cytotoxic agents, gowns and gloves shall be worn.
- (b) When compounding sterile products from one or more non-sterile ingredients the following standards must be met:
 - (1) Cleanroom garb consisting of a low-shedding coverall, head cover, face mask, and shoe covers must be worn inside the designated area at all times.
 - (2) Cleanroom garb must be donned and removed outside the designated area.
 - (3) Hand, finger, and wrist jewelry must be eliminated. If jewelry cannot be removed then it must be thoroughly cleaned and covered with a sterile glove.
 - (4) Head and facial hair must be kept out of the critical area or be covered.
 - (5) Gloves made of low-shedding materials are required.
- (c) The requirements of this subdivision do not apply if a barrier isolator is used to compound sterile injectable products from one or more non-sterile ingredients.

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.5. Training of Staff, Patient, and Caregiver.

(a) Consultation shall be available to the patient and/or primary caregiver concerning proper use of ~~parenterals~~ sterile injectable products and related supplies furnished by the pharmacy.

(b) The pharmacist-in-charge shall be responsible to ensure all pharmacy personnel engaging in compounding sterile injectable drug products ~~parenteral solutions~~ shall have training and demonstrated competence in the safe handling and compounding of sterile injectable products, ~~parenteral solutions~~ including cytotoxic agents if the pharmacy compounds products with cytotoxic agents.

(c) Records of training and demonstrated competence shall be available for each individual and shall be retained for three years beyond the period of employment.

(d) The pharmacist-in-charge shall be responsible to ~~insure~~ ensure the continuing competence of pharmacy personnel engaged in compounding sterile injectable products ~~parenteral solutions~~.

(e) Pharmacies that compound sterile products from one or more non-sterile ingredients must comply with the following training requirements:

1) The pharmacy must establish and follow a written program of training and performance evaluation designed to ensure that each person working in the designated area has the knowledge and skills necessary to perform their assigned tasks properly. This program of training and performance evaluation must address at least the following:

(A) Aseptic technique.

(B) Pharmaceutical calculations and terminology.

(C) Sterile product compounding documentation.

(D) Quality assurance procedures.

(E) Aseptic preparation procedures.

(F) Proper gowning and gloving technique.

(G) General conduct in the controlled area.

(H) Cleaning, sanitizing, and maintaining equipment used in the controlled area.

(I) Sterilization techniques.

(J) Container, equipment, and closure system selection.

(2) Each person assigned to the controlled area must successfully complete practical skills training in aseptic technique and aseptic area practices. Evaluation must include written testing and a written protocol of periodic routine performance checks involving adherence to aseptic area policies and procedures. Each person's proficiency and continuing training needs must be reassessed every 12 months. Results of these assessments must be documented and retained in the pharmacy for three years.

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.6. Disposal of Waste Material.

Pharmacies ~~providing parenteral services~~ compounding sterile injectable products shall have written policies and procedures for the disposal of infectious materials and/or materials containing cytotoxic residues. The procedures shall include cleanup of spills and shall be in conformance with local health jurisdiction. ~~The pharmacy shall ensure the return of such materials or shall communicate the proper destruction of such materials to the caregiver.~~

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.7. Quality Assurance and Process Validation.

(a) There shall be a documented, ongoing quality assurance program that monitors personnel performance, equipment, and facilities. The end product shall be examined on a periodic sampling basis as determined by the pharmacist-in-charge to assure that it meets required specifications. The Quality Assurance Program shall include at least the following:

- ~~(a)~~ (1) Cleaning and sanitization of the parenteral medication preparation area.
- ~~(b)~~ (2) Written documentation that the end product has been tested on a periodic sampling basis for microbial contamination and steps taken in the event that testing for contamination proves positive.
- ~~(c)~~ ~~If manufacturing of parenteral products is performed using nonsterile chemicals, extensive end product testing must be documented prior to the release of product from quarantine. This process must include testing for sterility and pyrogens.~~
- ~~(d)~~ (3) The storage of compounded sterile injectable ~~parenteral~~ products in the pharmacy and periodic documentation of refrigerator temperature.
- ~~(e)~~ (4) Steps to be taken in the event of a drug recall.
- ~~(f)~~ (5) Written justification of the chosen expiration dates for compounded sterile injectable ~~parenteral~~ products.

(b) Each individual involved in the preparation of sterile injectable products from one or more non-sterile ingredients must successfully complete a validation process on technique before being allowed to prepare sterile products. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used in place of the actual product used during sterile preparation. The validation process shall be representative of all types of manipulations, products and batch sizes the individual is expected to prepare. The same personnel, procedures, equipment, and materials are to be used in the validation process. Completed medium samples must be incubated. If microbial growth is detected, then the sterile preparation process must be evaluated, corrective action taken, and the validation process repeated. Personnel competency must be revalidated at least every twelve months, whenever the quality assurance program yields an unacceptable result, when the compounding process changes, equipment used in the compounding of sterile products is repaired or replaced, the facility is modified in a manner that affects airflow or traffic patterns, or whenever improper aseptic techniques are observed. Revalidation must be documented.

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Repeal Section 1751.8. Policies and Procedures.

~~Written policies and procedures associated with the pharmacy's preparation and dispensing of parenteral products shall include, but not be limited to:~~

- ~~(a) Compounding and labeling of intravenous admixtures.~~
- ~~(b) Administration of intravenous therapy.~~
- ~~(c) Equipment and supplies.~~
- ~~(d) Training of staff, patient and caregiver.~~
- ~~(e) Procedures for handling cytotoxic agents.~~

- ~~(f) Quality assurance program.~~
- ~~(g) Recordkeeping requirements.~~

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

Amend Section 1751.9. Reference Materials.

There shall be current and appropriate reference materials regarding the compounding of sterile injectable products located in or immediately available to the pharmacy.

~~Such references shall include information on:~~

- ~~(a) The drugs and chemicals used in parenteral therapy services and~~
- ~~(b) All parenteral therapy, manufacturing, dispensing, distribution, and counseling services provided.~~

NOTE:

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

PATRICIA HARRIS
Executive Officer

DATE